

APPENDIX A

1. An isolated nucleic acid molecule encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence which is an alternative splice form of a transcript of a B7-1 or B7-2 T cell costimulatory molecule gene, the nucleotide sequence being a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and being represented by a formula A-B-C-D-E, wherein

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a B7-1 or B7-2 signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes an B7-1 or B7-2 immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T B7-1 or B7-2 cell costimulatory molecule gene, wherein the at least one third exon encodes an B7-1 or B7-2 immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a B7-1 or B7-2 transmembrane domain, and

E comprises a nucleotide sequence of at least one fifth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a B7-1 or B7-2 cytoplasmic domain,

with the proviso that E is not the nucleic acid sequence shown in SEQ ID NO:25, E is not the nucleic acid sequence shown in SEQ ID NO:27, E is not the nucleic acid sequence shown in SEQ ID NO:29 and E is not the nucleic acid sequence shown in SEQ ID NO:31.

2. The isolated nucleic acid molecule of claim 1 which is a cDNA.

3. The isolated nucleic acid molecule of claim 2 which comprises a coding region of the cDNA.
4. The isolated nucleic acid molecule of claim 1, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-1.
5. The isolated nucleic acid molecule of claim 4, wherein B7-1 is murine.
6. The isolated nucleic acid molecule of claim 4, wherein B7-1 is human.
7. The isolated nucleic acid molecule of claim 5, wherein E comprises a nucleotide sequence shown in SEQ ID NO:4.
8. The isolated nucleic acid molecule of claim 5, wherein E comprises a nucleotide sequence encoding an amino acid sequence shown in SEQ ID NO:5.
9. An isolated nucleic acid encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 and which is an alternative splice form of a transcript of the a B7-1 or B7-2 T cell costimulatory molecule gene having
 - at least one first exon encoding a B7-1 or B7-2 first cytoplasmic domain comprising a nucleotide sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31, and
 - at least one second exon encoding a B7-1 or B7-2 second cytoplasmic domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the B7-1 or B7-2 second cytoplasmic domain andsaid nucleic acid molecule being a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22.
10. The isolated nucleic acid molecule of claim 9 which comprises a coding region of a cDNA.
11. The isolated nucleic acid molecule of claim 9 which does not comprise a nucleotide sequence encoding the first cytoplasmic domain.

12. The isolated nucleic acid molecule of claim 9 wherein the T cell costimulatory molecule gene is B7-1.
13. The isolated nucleic acid molecule of claim 12 wherein B7-1 is murine.
14. The isolated nucleic acid molecule of claim 12 wherein B7-1 is human.
15. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:1.
16. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:3.
17. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and encoding a cytoplasmic domain derived from a B7-1 or B7-2 protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:4.
30. A recombinant expression vector comprising the nucleic acid molecule of claim 15.
31. A host cell which contains the recombinant expression vector of claim 30.
33. An isolated nucleic acid molecule encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence which is an alternative splice form of a transcript of a B7-1 or B7-2 T cell costimulatory molecule gene, the nucleotide sequence being a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 represented by a formula A-B-C-D-E, wherein

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a B7-1 or B7-2 signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes a B7-1 or B7-2 immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one third exon encodes a B7-1 or B7-2 immunoglobulin constant region-like domain,

D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a B7-1 or B7-2 transmembrane domain, and

E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a B7-1 or B7-2 cytoplasmic domain,

with the proviso that A is not the nucleic acid sequence shown in SEQ ID NO:33, A is not the nucleic acid sequence shown in SEQ ID NO:35, A is not the nucleic acid sequence shown in SEQ ID NO:37, A is not the nucleic acid sequence shown in SEQ ID NO:39 and A is not the nucleic acid sequence shown in SEQ ID NO:41.

34. The isolated nucleic acid molecule of claim 33 which is a cDNA.

35. The isolated nucleic acid molecule of claim 34 which comprises a coding region of the cDNA.

36. The isolated nucleic acid molecule of claim 33, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-2.

37. The isolated nucleic acid molecule of claim 36, wherein B7-2 is murine.

38. The isolated nucleic acid molecule of claim 36, wherein B7-2 is human.

39. The isolated nucleic acid molecule of claim 37, wherein A comprises a nucleotide sequence shown in SEQ ID NO:14.

40. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 and which is an alternative splice form of a transcript of a B7-1 or B7-2 T cell costimulatory molecule gene having

at least one first exon encoding a B7-1 or B7-2 first signal peptide domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37 SEQ ID NO:39 and SEQ ID NO:41, and

at least one second exon encoding a B7-1 or B7-2 second signal peptide domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second signal peptide domain.

41. The isolated nucleic acid molecule of claim 40 which comprises a coding region of a cDNA.

42. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and which encodes a B7-1 or B7-2 protein which binds to CD28 or CTLA4, wherein said nucleic acid molecule comprises a nucleotide sequence shown in SEQ ID NOs: 4 and 14.

43. The isolated nucleic acid molecule of claim 40 wherein the T cell costimulatory molecule gene is B7-2.

44. The isolated nucleic acid molecule of claim 43 wherein B7-2 is murine.

45. The isolated nucleic acid molecule of claim 43 wherein B7-2 is human.

46. An isolated nucleic acid molecule encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:12.

47. An isolated nucleic acid molecule encoding a signal peptide domain derived from a B7-1 or B7-2 protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:14.

60. A recombinant expression vector comprising the nucleic acid molecule of claim 46.

61. A host cell which contains the recombinant expression vector of claim 60.

63. An isolated nucleic acid molecule encoding a B7-1 or B7-2 protein comprising a contiguous nucleotide sequence derived from at least one B7-1 or B7-2 T cell costimulatory molecule gene, the nucleotide sequence being a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and being represented by a formula A-B-C-D, wherein

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin constant region-like domain,

C comprises a nucleotide sequence of at least one third exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

D comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

64. The isolated nucleic acid molecule of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:8.

65. The isolated nucleic acid molecule of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:10.

69. An isolated nucleic acid molecule which is a naturally occurring variant of the nucleotide sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and encoding a B7-1 or B7-2 protein comprising a contiguous nucleotide sequence derived from at least one B7-1 or B7-2 T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

D comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

70. The isolated nucleic acid molecule of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:62.

71. The isolated nucleic acid molecule of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:64.

75. A recombinant expression vector comprising the nucleic acid molecule of claim 69.

76. A host cell which contains the recombinant expression vector of claim 75.

77. An isolated nucleic acid molecule encoding a B7-1 or B7-2 protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence which is an alternative splice form of a transcript of a B7-1 or B7-2 T cell costimulatory molecule gene, the nucleotide sequence being a naturally occurring variant of the nucleotide

sequence shown in SEQ ID NO:18 or SEQ ID NO:22 and being represented by a formula A-B-C-D-E, wherein:

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a B7-1 or B7-2 signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes a B7-1 or B7-2 immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one third exon encodes a B7-1 or B7-2 immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a B7-1 or B7-2 transmembrane domain, and

E comprises a nucleotide sequence of at least one fifth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a B7-1 or B7-2 cytoplasmic domain,

with the proviso that E is not the nucleic acid sequence shown in SEQ ID NO:25, E is not the nucleic acid sequence shown in SEQ ID NO:27, E is not the nucleic acid sequence shown in SEQ ID NO:29 and E is not the nucleic acid sequence shown in SEQ ID NO:31; or wherein

A comprises a nucleotide sequence of at least one first exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one first exon encodes a B7-1 or B7-2 signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one second exon encodes a B7-1 or B7-2 immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one third exon encodes a B7-1 or B7-2 immunoglobulin constant region-like domain,

D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a B7-1 or B7-2 T cell costimulatory molecule gene,

wherein the at least one fourth exon encodes a B7-1 or B7-2 transmembrane domain, and

E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a B7-1 or B7-2 T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a B7-1 or B7-2 cytoplasmic domain,

with the proviso that A is not the nucleic acid sequence shown in SEQ ID NO:33, A is not the nucleic acid sequence shown in SEQ ID NO:35, A is not the nucleic acid sequence shown in SEQ ID NO:37, A is not the nucleic acid sequence shown in SEQ ID NO:39 and A is not the nucleic acid sequence shown in SEQ ID NO:41.